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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,259	02/20/2004	Kenichiro Hasumi	358690-00005-1	7322

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,259	HASUMI ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/25/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *3-5,7,8 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/30/04, 10/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and amendment, filed on 25 January 2006.

Election/Restrictions

Applicant elects the species of prostate specific antigen, claim 6 from the genus of antigens as exemplified by claims 3-8. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 12-15 have been newly added and are asserted by Applicant to read on the elected embodiment. However, these new claims will not be examined because they are directed to different products (supernatant and activated cultured cells) that are distinct from the method claimed in claims 1-11. The claimed method can be practiced with other materially different products such as Freud's adjuvant. See MPEP § 806.05(h).

Claims 1-15 are pending. Claims 3-5, 7, 8, and 12-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species. Claims 1, 2, 6, and 9-11 are examined in the instant application.

Information Disclosure Statement

Two initialed and dated copy of Applicant's IDS form 1449, filed 30 August 2004 and 24 October 2005, are attached to the instant Office action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1 and 6 read on a method for enhancing an immune response to a prostate-specific antigen in a mammal comprising administering lymphocyte conditioned media (LCM) in combination with the antigen to the mammal.

The guidance presented in the specification is limited to the preparation of LCM, the cytokine and chemokine analysis of the LCM, and an *in vitro* antigen stimulation assay of human PBMCs. An *in vitro* cell culture detection of cytokines and chemokines after the addition of tetanus toxoid is nowhere near a clinical indication of the effectiveness of this LCM for the claimed method of enhancing an immune response to a prostate-specific antigen in a mammal like human, but a working hypothesis or speculation, because an *in vitro* system is over-simplified compared to the body of a mammal and is not predictive of, nor correlate with the complex nature immune systems in humans. Due to the highly unpredictable and complex nature of immunology,

extrapolating from *in vitro* models to mammals without *in vivo* validation is hazardous; likewise, extrapolating results from one antigen to a nonanalogous antigen is unpredictable. A prostate-specific antigen is an endogenous mammalian protein whereas a tetanus toxoid is an isolated bacterial protein. Therefore, one skilled in the art would attribute the unpredictable state of the art of immune response elicited by these two antigens to their unrelated origins.

Given the difference between the two antigens and the gap between *in vitro* and *in vivo* immune response results, the clinical relevance of the disclosed measurements of cytokines and chemokines in the LCM in the instant application is uncertain. One skilled in the art would be burdened with an undue quantity of *in vivo* experiments in order to make and use the current invention since the applicants have not provided any clear-cut evidence to demonstrate the effectiveness of the claimed LCM in enhancing immune responses to co-administered antigen. Absent working examples and specific teachings of the clinical efficacy of the LCM, those in the art would not be able to use the claimed method.

Considering the lack of data or working examples in the specification, the broad scope of the claims, and the complex state and unpredictable nature of the art, the Applicant has not provided sufficient information to enable those skilled in the art to practice the claimed method *in vivo* for an entirely different antigen without undue experimentation. The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Baxevanis *et al.* (1997).

Claim 1 reads on a method of enhancing an immune response to an antigen in human PBMCs comprising administering lymphocyte conditioned media in combination with said antigen to the cell culture.

Baxevanis *et al.* teach a method of induction of anti-tumor lymphocytes in cancer patients' PBMCs by adding supernatants collected from cultures of healthy donor-derived PBMCs stimulated with anti-CD3 monoclonal antibody. See entire document.

Thus, the instant invention is anticipated by Baxevanis *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. §103(a) as being unpatentable over Baxevanis *et al.* (1997) in view of Santamaria *et al.* (1990).

The instant invention is further limited to using LCM derived from naïve T cells cultured with anti CD3/CD28-coated beads.

The relevance of Baxevanis *et al.* is stated above. Baxevanis *et al.* teach immobilizing anti-CD3 monoclonal antibodies on the surface of flasks but do not teach coating anti-CD3 on to the beads.

However, Santamaria *et al.* teach the use of polystyrene particles coated with anti-CD3 monoclonal antibodies and stresses the efficiency of the beads. See Abstract.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the flask-immobilized anti-CD3 of Baxevanis *et al.* to the bead-immobilized anti-CD3 as suggested by Santamaria *et al.* with a reasonable expectation of success, absent unexpected results to the contrary. The motivation to do so is provided by Santamari *et al.*, who teach the ease of expansion of T cells using anti-CD3 coated polystyrene beads even in the absence of specific antigens.

Thus, claims 1 and 2 are *prima facie* obvious over the combined teachings of Baxevanis *et al.* and Santamaria *et al.*

Claims 1 and 9-11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Baxevanis *et al.* (1997) in view of Setaluri *et al.* (2002).

The instant invention is further limited to the dosage, and the administration route and schedule.

The relevance of Baxevanis *et al.* is set forth above. Baxevanis *et al.* do not teach the further limitations. However, Setaluri *et al.* teach the dosage calculation and

the administration of a tumor antigen hourly, daily, weekly, monthly, or yearly, by intramuscular or intravenous injection. See column 10, paragraphs 90 and 92.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the dosage calculation, administration route and schedule taught by Setaluri *et al.* with the method of induction of anti-tumor lymphocytes taught by Baxevanis *et al.* with a reasonable expectation of success, absent unexpected results to the contrary. The motivation to do so is provided by Setaluri *et al.*, who teach the therapeutic efficacy of exogenous compounds and clearly state the standard pharmaceutical procedures for administration of an anti-tumor antigen.

Thus, claims 1 and 9-11 are *prima facie* obvious over the teachings of Baxevanis *et al.* in view of Setaluri *et al.*

Remarks

No claim is allowable.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D., whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902.

Louise Humphrey, Ph.D.
Patent Examiner
10 February 2006

JEFFREY STUCKER
PRIMARY EXAMINER